remainder 5–10:1 stereoselection. Desired stereoisomers at C4–C10 were prepared selectively in every case. These and previous results provide firm evidence that macrocyclic stereocontrol is a general and effective strategy that can be of significant value in complex synthesis. While one may argue that the approach lacks convergency since it postpones certain construction steps until after the coupling of major fragments, the objection is not a serious one: only those few reactions that set stereochemistry need be postponed.

The high stereoselection commonly produced in the kinetic reactions of macrocycles is related to the conformational preferences of the reaction transition states; however, the details of such preferences in complex structures like those described above are as yet unclear. Our next goal is to find a reliable way to predict macrocyclic diasteroselection so that macrocyclic stereocontrol strategies may be used rationally in complex synthesis and so that the mechanism of the stereoselection may be elucidated.[10]

Acknowledgment. We are grateful to Dr. A. K. Ganguly of Schering Corp. for a generous supply of rosaramicin and to Diana Burman for assisting in the preparation of early intermediates.

Supplementary Material Available: Outlines of preparations of **3** and naturally derived **1b**, ORTEP crystal structures for **4** and **5a**, and full spectral data for **1b–10** (13 pages). Ordering information is given on any current masthead page.

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Isolation and X-ray Crystal Structure of the Cuprate Complex $[Li_2Cu_3Ph_6]_2[Li_4Cl_2(Et_2O)_{10}]$: The First X-ray Structural Characterization of an Anionic Organocopper-Lithium Cluster

Håkon Hope, Douglas Oram, and Philip P. Power*

Department of Chemistry, University of California
Davis, California 95616

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The widespread use of lithium organocuprates as reagents in organic synthesis has led to considerble interest in their structures.[1] Solution ^1H NMR and molecular weight determinations have indicated that, depending on how the cuprate is prepared, species such as $LiCuR_2$, $LiCu_2R_3$, Li_2CuR_3, or $Li_2Cu_3R_5$ are present.[2] However, none of these interesting aggregates has been isolated where R is a simple alkyl or aryl group. The most relevant published work has concerned the dimeric species $[Li_2Cu_2Ar_4]$[3] involving the chelating group $2\text{-}Me_2NCH_2C_6H_4^-$. However, the nitrogen donors undoubtedly play a significant role in the structure and a direct structural comparison to complexes involving methyl or unsubstituted phenyl groups is open to question. The only X-ray structural characterizations of cuprate complexes involve the species $[Cu(Mes)_2][Cu(dppe)_2]$[4] (Mes = mesityl), in which two aryl groups are σ-bound to a linear copper(I) and the cluster $[Li(THF)_4][Cu_5Ph_6]$.[5] The former was obtained by the disproportionation of [Cu(Mes)] with dppe and does not contain lithium while the latter, although isolated from a lithium cuprate solution, has a Li:Cu ratio of 1:5 rather than the usual 1:1 ratio.

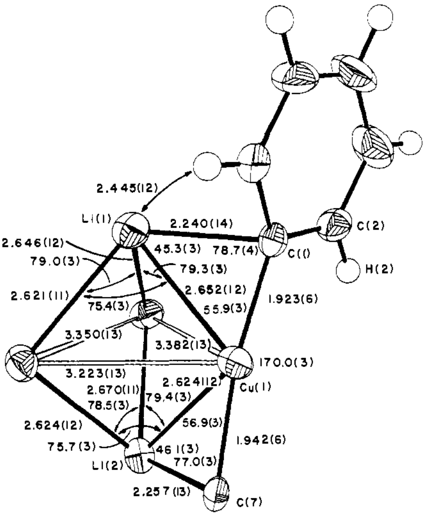

Figure 1. Thermal ellipsoid plot of the anion of **1**. Five of the phenyl groups have been omitted for clarity.

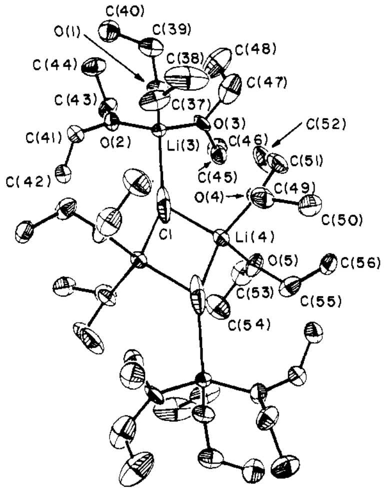

Figure 2. Thermal ellipsoid plot of the cation of **1**. Hydrogen atoms have been omitted for clarity.

In this paper we report the first X-ray crystal structure of a cluster involving a framework of both lithium and copper atoms, prepared in a fortuitous manner. We were examining crystalline products from cuprate solutions, derived from CuCN[6] and 2 equiv of LiPh in ether, with the object of explaining their high reactivity toward various organic substrates.[7] These solutions invariably afforded a mixture of yellow and colorless crystals after filtration and cooling to −20 °C. The X-ray data[8] for the yellow crystals revealed that the compound crystallizes as $[Li_2Cu_3Ph_6]_2[Li_4Cl_2(Et_2O)_{10}]$ (**1**) (Figures 1 and 2). The presence of chloride

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[8] A yellow crystal of **1** of dimensions 0.40 × 0.40 × 0.37 mm was mounted on a Syntex $P2_1$ diffractometer equipped with a graphite monochromator. With Mo Kα (λ = 0.71069 Å) and the crystal cooled to 140 K, crystal data were as follows: monoclinic $P2_1/n$; a = 13.214 (8) Å, b = 18.20 (1) Å, c = 24.42 (2) Å, β = 97.17 (5)°; Z = 2; μ = 11.75 cm^{-1}. Data were collected to $2\theta_{max}$ of 47° with an ω scan technique. A total of 8618 unique data were collected of which 5287 had $I > 2\sigma(I)$. Scattering factors and corrections for anomalous scattering were from Vol. IV of the International Tables. The structure was solved by direct methods. Computer programs are those of SHELXTL, Version 3, July 1981 package. The absorption correction was applied. The non-hydrogen atoms were anisotropically refined (652 parameters) and the final R factors are R = 0.0632 and R_w = 0.0487.

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in the product arose from Cl$^-$, which was present as a 6–7% impurity of the CuCN starting material. We estimated this percentage from the yield (ca. 20%) of **1**, and this figure was later corroborated by elemental analysis on the commercial CuCN used.[9] The colorless crystals obtained in ca. 25% yield from the same solutions had cell constants identical with the crystals obtained from the reaction of CuBr with 2 equiv of LiPh. The structure of this compound has not been completely solved due to disorder problems but is probably a cubane structure of formula $[(\mathrm{LiCuPh_2{\cdot}Et_2O})_4]$.[11]

The anion of **1** (Figure 1) contains a trigonal bipyramid with two lithium (apical) and three copper (equatorial) atoms. Each Li–Cu vector is bridged by a phenyl group. The framework is very close to that described for $[\mathrm{Cu_5Ph_6}]^-$ but the Li⋯Li distance is 3.63 (3) Å, so that the TBP cluster is not as "squashed" as it is in the $[\mathrm{Cu_5Ph_6}]^-$ ion.[5] The close structural relationship shows that replacement of two copper atoms by lithium allows retention of the basic architecture, which has also been seen in related systems.[10] The Cu–C distances (typical value 1.929 (6) Å) are very close to those found in $[\mathrm{Cu(Mes)_2}]^-$,[4] $[\mathrm{Cu_5Ph_6}]^-$,[5] and $[\mathrm{Li(12\text{-}crown\text{-}4)_2}][\mathrm{CuPh_2}]$.[11] The Li–C distances in **1** are somewhat long (typical value 2.240 (14) Å), but they are shorter than those found in $[(\mathrm{LiPh{\cdot}Et_2O})_4]$.[12] The Cu–Cu distances (ca. 3.3 Å) preclude significant metal–metal bonding at the equatorial edges. A curious feature of **1** arises from its stoichiometry. If the ethers are disregarded the formula may be written as $[(\mathrm{LiCuPh_2})_3(\mathrm{LiCl})]$. Together with the compound $[(\mathrm{LiCuPh_2})_4]$ this bears a stoichiometric resemblance (again ignoring the ethers) to the halide-free and halide-rich phenyllithium species $[(\mathrm{LiPh})_4]$ and $[(\mathrm{LiPh})_3\mathrm{LiBr}]$. Although there is no structural correspondence between the two copper compounds, it may be that the presence of a different species such as **1** in solution may account, in part, for the difference in reactivity between cuprates derived from CuBr and from CuCN contaminated by Cl$^-$.

The structure of the cation (Figure 2) is also of interest as it is the first structure of a lithium halide aggregate (outside of the lithium halides themselves). Various studies (including EXAFS)[13] have shown that lithium halides exist as tetramers in ether and as dimers in ethylene carbonate. The structure of the cation indicates that it may be possible to crystallize these and other complexes. The cation structure consists of a planar core of two Li and two Cl atoms; each Cl atom is also coordinated to a terminal Li. All the Li atoms are four-coordinate due to further coordination to either two or three ether molecules. The Li–O distances, ca. 1.96 Å, are close to those found in other etherates.[12,14] The terminal Li–Cl distance, 2.697 (12) Å, is longer than either of the bridging distances, 2.537 (12) and 2.505 (12) Å. This is probably due to the terminal Li atoms being more electron rich by coordination to one more ether instead of a Cl$^-$ ion, which is a poorer electron donor.

Studies to isolate and structurally characterize other lithium organocuprates are in progress.

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Supplementary Material Available: Full tables of atom coordinates and bond distances and angles of **1** (4 pages). Ordering information is given on any current masthead page.

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(9) Chloride analyses in this laboratory and also: Bertz, S. H., personal communication.

(10) For example, in $\mathrm{Cu_4Ar_4}$,[3] $\mathrm{Li_2Cu_2Ar_4}$,[3] or $\mathrm{Cu_2Au_2Ar}$ (Ar = 2-$\mathrm{Me_2NCH_2C_6H_4}$). van Koten, G.; Schaap, C. A.; Jastrzebski, J. T. B. H.; Noltes, J. *J. Organomet. Chem.* **1980**, *186*, 427–445. Noltes, J. G. *Philos. Trans. R. Soc. London, Ser. A* **1982**, *308*, 35–45.

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Sensitivity-Enhanced NMR Detection of Nonprotonated ^{15}N Nuclei

Ad Bax,* Chien-Hua Niu, and David Live†

Laboratories of Chemical Physics
and Biochemical Pharmacology
National Institute of Arthritis, Diabetes, and
Digestive and Kidney Diseases
National Institutes of Health
Bethesda, Maryland 20205

Received November 14, 1983

We wish to demonstrate that a simple modification of the INEPT experiment[1-3] allows polarization of nonprotonated ^{15}N nuclei in peptides. This selective polarization method yields a large enhancement in sensitivity and also correlates the ^{1}H and ^{15}N shift, providing assignment information. It has been demonstrated in the past, that selective pulse polarization transfer (SPT) can give large sensitivity enhancement for both protonated and nonprotonated ^{13}C and ^{15}N resonances.[4-7] However, the SPT method is very difficult to use in the case of complex coupling networks and if couplings are not resolved and is therefore generally not easily applicable to the study of resonances of nonprotonated ^{15}N nuclei.

Several new methods have been introduced in recent years that allow polarization transfer from protons to the heteronucleus, for example, ^{15}N, using only nonselective pulses.[1-3,7,8] The INEPT experiment, first introduced by Morris and Freeman,[1] is the oldest of these methods. The refocused INEPT sequence[3] is set out in Figure 1. This sequence works very well for protonated ^{15}N nuclei, and transverse magnetization can be enhanced by a factor of nearly $\gamma_{^1\mathrm{H}}/\gamma_{^{15}\mathrm{N}} = 10$, compared with that created by a single 90° (^{15}N) pulse without NOE. The INEPT sequence usually fails if one wants to enhance magnetization of nonprotonated ^{15}N nuclei, by optimizing the duration of the delays, Δ, for a certain long-range coupling, $^{lr}J_{\mathrm{NH}}$. To clarify the advantages of our modification, we wish to comment first on why the regular INEPT experiment fails. First, if homonuclear proton coupling is present, significant dephasing of the protons occurs during the interval Δ_1 ($\approx 1/(2^{lr}J_{\mathrm{NH}})$), and the $90°_{\pm y}$ (^{1}H) pulse will create a large amount of homonuclear multiple quantum coherence.[8-10] This multiple quantum coherence cannot directly be transferred into ^{15}N transverse magnetization. Second, the multiplet components of the ^{15}N magnetization that has been transferred are in antiphase just after the 90° ^{15}N pulse. One therefore has to wait for a time Δ_2, of the order of $1/(2^{lr}J_{\mathrm{NH}})$, before proton decoupling can be started. If the ^{15}N nucleus is coupled to a number of protons, the ^{15}N signal will decay rapidly during this time, Δ_2, and little magnetization will be left when broad-band proton decoupling is started.

We propose the use of soft proton pulses (typical 90° flip angle $\approx$5 ms) in order to avoid the two problems mentioned above. If the proton pulses only affect one preselected proton, the dephasing due to homonuclear coupling will be refocused just before the second 90° proton pulse by the selective 180° pulse, applied at the midpoint of the interval, Δ_1. Therefore, no homonuclear multiple quantum coherence will be created by the second 90° (^{1}H) pulse, and all ^{1}H magnetization will be transfered to the ^{15}N nucleus, analogously to the case of a directly bonded ^{15}N–^{1}H pair, where a short value for Δ_1 can be used. The total precession of

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† The Rockefeller University, New York, NY 10021.

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